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CLINICAL STUDIES ASSESSING TRANSCATHETER AORTIC VALVE REPLACEMENT

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Introduction

Degenerative aortic stenosis is the most common acquired valvular heart disease in the developed countries, affecting more than 300,000 people in the United States alone.[1] Symptoms of aortic stenosis are latent until there is critical narrowing of the aortic valve that results in left ventricular hypertrophy, increased left ventricular diastolic pressure and left ventricle mass, and increased myocardial oxygen demand causing subendocardial ischemia.[2] Once symptoms develop, the prognosis changes dramatically unless the aortic stenosis is corrected.[2]

Surgical aortic valve replacement (sAVR) is the recommended therapy for patients with symptomatic aortic stenosis. The most recent American College of Cardiology and American Heart Association (ACC/AHA) guidelines for sAVR are found in Table 1.[3] It is important to note that none of these recommendations are based on evidence from large-scale, randomized clinical trials but instead rely on the expert opinion of experienced clinicians. The Society for Thoracic Surgery Predicted Risk of Mortality (STS-PROM) has been used to estimate 30-day mortality operative risk. Other surgical risk scores, such as the logistic EuroSCORE, while correlated with overall prediction of risk, are poorly calibrated to estimate precise sAVR mortality rates.[4]

Many patients cannot undergo sAVR due to excessive surgical risk, including porcelain aorta,[5, 6] hostile mediastinum, severe lung or liver disease, frailty, renal failure,[7-9] advanced age, and prior CABG,[10] among other factors,[11, 12] many of which are not included in current surgical risk assessment algorithms. In patients who are deemed unsuitable for sAVR due to comorbidities, transcatheter aortic valve replacement (TAVR) has been used as an alternative to relieve symptoms and extend life. Almost 50,000 patients have been treated worldwide with one of the two commercially approved TAVR devices, including the balloon-expandable Edwards SAPIEN Transcatheter Heart Valve (Edwards LifeSciences, Irvine, California) and the self-expanding CoreValve Revalving System (Medtronic, Minneapolis, Minnesota). A number of additional transfemoral and transapical devices are under evaluation.

The purpose of this report is to review the clinical trials used to evaluate TAVR in patients who are at higher risk for sAVR. The clinical evidence base includes both prospective registries and randomized clinical trials. Future trial designs evaluating TAVR in intermediate populations will also be discussed.

Table 1. ACC-AHA recommendations for surgical aortic valve replacement.[3]

Class	LOE	Recommendation
I	B	AVR is indicated for symptomatic patients with severe AS.
I	C	AVR is indicated for patients with severe AS undergoing coronary artery bypass graft surgery (CABG).
I	C	AVR is indicated for patients with severe AS undergoing surgery on the aorta or other heart valves.
I	C	AVR is recommended for patients with severe AS and LV systolic dysfunction (ejection fraction less than 0.50).
IIa	B	AVR is reasonable for patients with moderate AS undergoing CABG or surgery on the aorta or other heart valves.
IIb	C	AVR may be considered for asymptomatic patients with severe AS and abnormal response to exercise (e.g., development of symptoms or asymptomatic hypotension).
IIb	C	AVR may be considered for adults with severe asymptomatic AS if there is a high likelihood of rapid progression (age, calcification, and CAD) or if surgery might be delayed at the time of symptom onset.
IIb	C	AVR may be considered in patients undergoing CABG who have mild AS when there is evidence, such as moderate to severe valve calcification, that progression may be rapid.
IIb	C	AVR may be considered for asymptomatic patients with extremely severe AS (aortic valve area less than 0.6 cm^2, mean gradient greater than 60 mmHg, and jet velocity greater than 5.0 m per second) when the patient's expected operative mortality is 1.0% or less.
III	B	AVR is not useful for the prevention of sudden death in asymptomatic patients with AS who have none of the findings listed under the class IIa/IIb recommendations.

AS: aortic stenosis; AVR: aortic valve replacement; CABG: coronary artery bypass graft surgery; CAD: coronary artery disease; LOE: level of evidence; LV: left ventricular.

Extreme-Risk or Inoperable Patients for sAVR

Early clinical evaluation of TAVR included patients deemed unsuitable for sAVR. The logistic Euroscore was the primary risk algorithm used for reporting these series, but a number of specific clinical factors, including advanced age, prior CABG, cirrhosis, pulmonary disease and pulmonary artery hypertension, right ventricular failure, or mediastinal radiation were used for inclusion of patients in TAVR studies.

Balloon-Expandable TAVR Registries and Randomized Clinical Trials

The Edwards SAPIEN Transcatheter Heart Valve consists of a trileaflet bovine pericardial valve and a balloon-expandable, stainless-steel support frame. The SAPIEN valve has undergone clinical study in the United States in 23-mm and 26-mm sizes. It is placed by means of a 22-French (Fr) or 24-Fr sheath from the femoral artery or via the transapical approach using a modified frame and larger delivery sheath. A second-generation 18-Fr RetroFlex II delivery system and a 29-mm SAPIEN XT valve are both available outside the United States and are currently undergoing US-based clinical trials through the PARTNER II study.

A number of single-center series have evaluated the outcomes of TAVR using the Edwards SAPIEN system.[13] The largest of these is the SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry, which assessed the initial clinical results of TAVR in consecutive patients in Europe using the SAPIEN valve after commercialization; patients undergoing the transapical approach had a higher logistic EuroSCORE that those undergoing the transfemoral approach (29.1% versus 25.7%, respectively).[14] Short-term procedural success was observed in 93.8% of patients, with reported complications including stroke (2.5%), valve embolization (0.3%), and coronary obstruction (0.6%). Thirty-day mortality was 6.3% in transfemoral patients and 10.3% in transapical patients.[14] The SOURCE registry reported a total Kaplan Meier 1-year survival of 76.1% overall, with 72.1% for transapical patients and 81.1% for transfemoral patients.[14] At 1 year, 73.5% of surviving patients were in New York Heart Association (NYHA) class I or II.[14] The cause of late mortality was cardiac in 25.1%, noncardiac in 49.2%, and unknown in 25.7%.[14] The most frequent noncardiac causes of death were due to pulmonary complications (23.9%), renal failure (12.5%), cancer (11.4%), and stroke (10.2%).[14] Multivariable analysis identified logistic EuroSCORE, renal disease, liver disease, and smoking as variables with the highest hazard ratios for 1-year mortality.[14]

Two randomized clinical trials demonstrated the value of balloon-expandable TAVR in patients poorly suited for sAVR (Table 2). The PARTNER I-B study included 358 patients who were deemed inorperable and randomly assigned to standard therapy (including balloon aortic valvuloplasty) or transfemoral TAVR.[15] The primary endpoint, 1-year all-cause mortality (Kaplan-Meier analysis), was 30.7% with TAVR and 50.7% with standard therapy (hazard ratio with TAVI: 0.55; P <0.001).[15] The frequency of severe cardiac symptoms (New York Heart Association class III or IV) in 1-year survivors was lower in patients who had undergone TAVR than in those who had received standard therapy (25.2% versus 58.0%, P <0.001).[15] Major strokes were higher at 30 days in patients treated with TAVR (5.0% versus 1.1% in medically-treated patients, P = 0.06), and major vascular complications were also higher in patients undergoing TAVR (16.2% versus 1.1% in medically-treated

Table 2. Trial design for ongoing and completed studies for TAVR.

	Definition	Trial Design	Control	Number Pts	Primary Endpoint
Extreme-Risk or "Inoperable" Patients					
PARTNER I-B	>50% risk of death or irreversible morbidity at 30 days	Prospective, randomized 1:1	Medical Therapy including BAV	358	Rate of death from any cause over the duration of the trial Coprimary end point was the rate of a hierarchical composite of the time to death from any cause or the time to the first occurrence of repeat hospitalization
PARTNER II-B	>50% risk of death or irreversible morbidity at 30 days	Prospective, randomized 1:1	Medical Therapy including BAV	NR	1-year time to death, major stroke, and repeat hospitalization
US CoreValve	>50% risk of death or irreversible morbidity at 30 days	Prospective Registry	Performance Goal	487	1-year all-cause mortality and major stroke (versus performance goal)
High-Risk Surgical Patients					
PARTNER I A	>15% risk of 30-day death (with STS >8)	Prospective, randomized 1:1	SAVR	699	1-year all-cause mortality
US CoreValve	>15% risk of 30-day death	Prospective, randomized 1:1	SAVR	790	1-year all-cause mortality
Intermediate-Risk Patients					
PARTNER II A	STS PROM 4-8	Prospective, randomized 1:1	SAVR or SAVR-CABG	2000	2-year all-cause mortality and major stroke
SURTAVI	STS PROM >3 for OUS and >4 for US patients	Prospective, randomized 1:1	SAVR or SAVR-CABG	1200	2-year all-cause mortality and major stroke

Table 3. National registries with self-expanding CoreValve TAVR.

Registry	Age	Males, %	Logistic EuroSCORE	NYHA Class III-IV, %	Mean Gradient, mmHg	Vascular Complic, %	Stroke, %	PPM, %
Italian[19]	81±7.3	44	23±13.7	71.5	51.8±17	2.0	1.2	16.6
Belgian[20]	82±6	44	25±15	78	49±16	—	4	22.0
French[21]	82.5±5.9	48.5	24.7±11.2	74.6	46±15	7.5	4.5	25.7
Spanish[23]	78.6±6.7	45.4	16±13.9	58.4	55±14.3	5.6	0	35.2
UK[22]	83	52	20.3	74	—	4.0	4.3	26.0
German[24]	81.4±6.3	44.2	20.5±13.2	88.2	48.7±17	4.0	2.8	39.3
Australia-NZ[25]	82.7±7.7	59.3	18±12	84	51 ± 16	6.5	1.9	40.0

Complic: complications; NYHA: New York Heart Association; PPM: permanent pacemaker placement; TAVR: transcatheter aortic valve replacement

patients, P <0.001).[15] There was no deterioration in bioprosthetic valve functioning at 1 year, as assessed by evidence of stenosis or regurgitation on an echocardiogram.[15]

Cohort A of the PARTNER Trial randomly assigned 699 high-risk patients with severe aortic stenosis to undergo either transcatheter aortic valve replacement with a balloon-expandable bovine pericardial valve (using a transfemoral or transapical approach) or surgical replacement (Table 2).[16] The rates of death from any cause were 3.4% in the TAVR group and 6.5% in the sAVR group at 30 days (P = 0.07) and 24.2% and 26.8%, respectively, at 1 year (P = 0.44), a reduction of 2.6 percentage points in the TAVR group (P = 0.001 for noninferiority).[16] The rates of major stroke were 3.8% in the TAVR group and 2.1% in the sAVR group at 30 days (P = 0.20) and 5.1% and 2.4%, respectively, at 1 year (P = 0.07). At 30 days, major vascular complications were significantly more frequent with TAVR (11.0% versus 3.2%, P <0.001); adverse events that were more frequent after sAVR included major bleeding (9.3% versus 19.5%, P <0.001) and new-onset atrial fibrillation (8.6% versus 16.0%, P = 0.006).[16] More patients undergoing TAVR had an improvement in symptoms at 30 days, but by 1 year there was not a significant difference between groups.[16]

The PARTNER II (Cohort B) Trial is designed to determine the safety and effectiveness of the Edwards 18-Fr SAPIEN XT™ device and NovaFlex delivery system in inoperable patients with symptomatic critical aortic stenosis.[17] Patients will be randomized in a 2:1 fashion to the SAPIEN XT device or the SAPIEN RetroFlex III device.[17] The primary noninferiority endpoints are all-cause mortality, major stroke, and repeat hospitalization at 1 year.[17]

Self-Expanding TAVR Registries and Randomized Clinical Trials

The Medtronic CoreValve ReValving System (Medtronic, Inc., Minneapolis, MN) consists of a trileaflet porcine pericardial valve and a self-expanding nitinol support frame. The CoreValve is available for clinical study in the United States in 23-mm, 26-mm, 29-mm, and 31-mm sizes. It is placed by means of an 18-Fr sheath from the femoral artery or subclavian (axillary) arteries or via direct aortic access.

The 18-Fr Safety and Efficacy Study included 126 patients (logistic EuroSCORE = 23.4%) with severe aortic valve stenosis.[18] The overall technical success rate was 83.1%, and the 30-day all-cause mortality was 15.2%.[18] All-cause mortality was 38.1% at 2 years. There was a significant difference in 2-year mortality between moderate-risk and high-risk groups (27.8% versus 45.8%, respectively; P = 0.04), mainly attributable to an increased risk of noncardiac mortality among patients in the high-risk groups.[18] Hemodynamic results remained unchanged during follow-up (mean gradient: 8.5 ± 2.5 mmHg at 30 days and 9.0 ± 3.4 mmHg at 2 years).[18] Functional class improved in 80% of patients and remained stable over time. There was no incidence of structural valve deterioration.

A number of national registries have been developed to evaluate the safety and efficacy of the CoreValve TAVR (Table 3).[19-25] These registries have included 2,156 patients, and a preliminary meta-analysis of these registries has been reported.[19-25] Although there were no consistent definitions, procedure success rates ranged from 92.6 to 98%, and 30-day mortality rates ranged from 84.9 to 92.1%.[19-25]

The United States CoreValve Extreme Risk Pivotal Registry has completed enrollment of 487 patients deemed to have a predicted 30-day surgical mortality risk or irreversible serious morbidity risk that exceeds 50%. The primary endpoint, the combination of 1-year all-cause mortality or major stroke, will be compared with a performance goal determined from the PARTNER B study and contemporary balloon valvuloplasty registries. In addition, up to 200 patients diagnosed as extreme risk but whose iliofemoral anatomy precludes placement of an 18-Fr sheath will undergo either an axillary or direct aortic approach described below.

The CoreValve US Pivotal Trial includes 790 high-risk patients deemed to have an estimated 30-day mortality of between 10% and 15% due to the presence of comorbidities. Patients are assigned in 1:1 fashion to either TAVR or to sAVR. The primary endpoint, 1-year all-cause mortality, will assess the noninferiority of TAVR with sAVR. Up to 20% of patients can be treated using a noniliofemoral approach. Patients with significant residual coronary artery disease are excluded as coronary artery bypass surgery is allowed at the time of sAVR.

An important aspect of these studies is the inclusion of patients who are treated with an alternative noniliofemoral access route. In patients with a minimal lumen iliofemoral diameter of <6.0 mm in a noncalcified vessel and <7.0 mm in a calcified vessel, those with aneurysmal dilatation of the abdominal aorta or with prior surgical or percutaneous aneurysm repair will be treated using either the subclavian (axillary) or direct aortic approaches.[26-30]

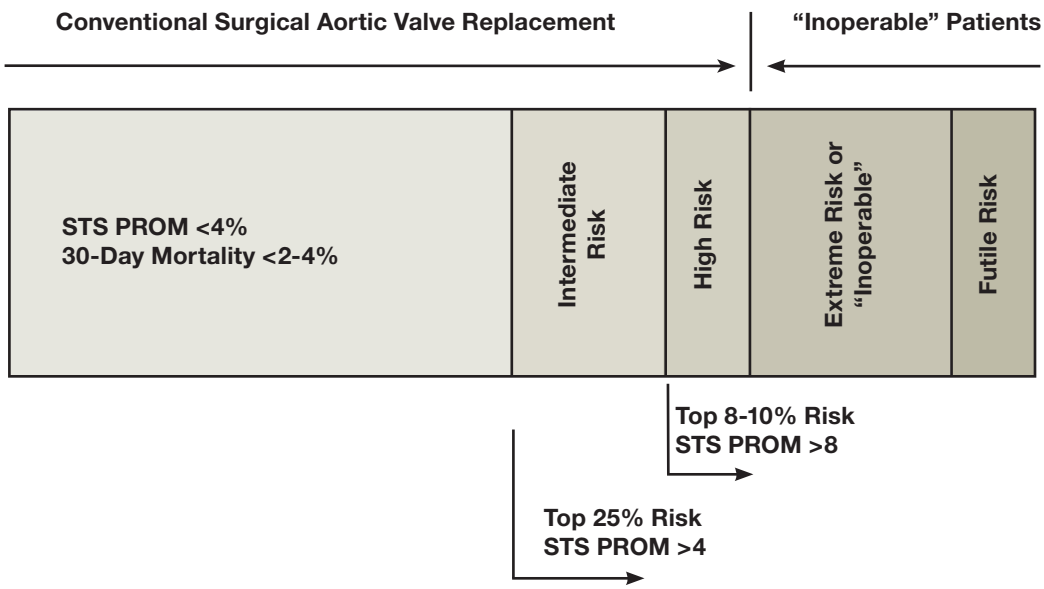

Figure 1. Spectrum of surgical risk in patients with aortic stenosis.

The ADVANCE Registry was a prospective, multicenter, observational study in 1,015 patients undergoing TAVR with CoreValve in Europe. CoreValve implantation was performed in 996 patients. In a preliminary report of this registry, the primary endpoint, a composite of major adverse cardiac and cerebrovascular events at 30 days, occurred in 8.3% of patients, with a 30-day all-cause mortality rate of 4.3%.[31]

Intermediate-Risk Patients

With the noninferiority of TAVR demonstrated in patients at high-risk for sAVR, there is general interest in expanding the clinical trial portfolio to include lower-risk patients (Figure 1). An STS-PROM >4 comprises the highest 25% risk of patients currently undergoing sAVR, and an STS-PROM >3 identifies the highest 33% risk.[17] Two studies have been designed to address this population of intermediate-risk patients.

The PARTNER II Cohort A Trial is a noninferiority study of up to 2,000 patients with severe, symptomatic aortic valve stenosis who have an elevated risk for traditional open-heart surgery (STS-PROM ≥4).[17] Patients without coronary artery disease will be randomly assigned to TAVR (SAPIEN XT) or sAVR.[17] Patients with coronary artery disease will be randomly assigned to TAVR (SAPIEN XT), percutaneous coronary intervention or sAVR, and coronary artery bypass graft surgery. Those undergoing TAVR will be treated with either a transfemoral or transapical approach. The primary endpoint to be evaluated is a composite of death and major stroke at 2 years, with secondary endpoints that include valve performance and quality-of-life indicators.[17]

The SURgery and Transcatheter Aortic Valve Implantation (SURTAVI) trial is an international, multicenter, randomized clinical study that plans to enroll up to 2,000 patients in Europe and the United States to evaluate safety and efficacy of TAVR versus surgical AVR. The study will evaluate a broader range of patients including those with intermediate risk for undergoing sAVR. Patients outside the United States will have an STS-PROM >3, and patients enrolled in the United States will have an STS-PROM >4. Clinical centers with previous experience in TAVR will be eligible to participate in the study. SURTAVI will use a heart team approach that includes an interventional cardiologist and cardiac surgeon. The study's primary endpoint is 2-year all-cause mortality and major stroke. Secondary endpoints include valve failure, endocarditis, and regression of the left ventricle and need for PPMI.

Clinical Condition
• Aortic valve is a congenital unicuspid or bicuspid valve; or is non-calcified.
• Pre-existing prosthetic heart valve in any position, prosthetic ring, or severe (greater than 3+) mitral insufficiency.
• Severe ventricular dysfunction with LVEF <20.
• Renal insufficiency (Creatinine >3.0) and/or end-stage renal disease requiring chronic dialysis.
• Low-gradient low-output aortic stenosis.
• Patients who have significant associated valvular lesions that cannot be treated surgically.
Recommended Endpoints
• Mortality
• Functional improvement per NYHA functional class
• Stroke
• Other major adverse cardiovascular events
• Length of hospital stay

Table 4. STS-ACC recommendations for continued evidence development.[31] STS: Society of Thoracic Surgeons; ACC: American College of Cardiology; LVEF: left ventricular ejection fraction

Continuing Evidence Development

The STS and American College of Cardiology have recommended that additional clinical study be performed to determine the value of TAVR in patients who are not included in the randomized trials and registries (Table 4).[32] For the majority of patients who are poor candidates for sAVR, there is little question of the profound clinical benefit from undergoing TAVR. Implementation of a multidisciplinary team is essential for appropriate patient selection. Several complications with TAVR require careful procedural attention during the periprocedural period, including stroke,[33] vascular complications, perivalvular regurgitation,[34, 35] and the need for permanent pacemaker placement.[36] New TAVR designs will be available to potentially lower these complication rates (Table 4). In addition, multidetector CT imaging has been very valuable in predicting the appropriate valve size and guiding vascular access.

Based on growing evidence, TAVR is now recognized as superior to medical therapy in patients who are not suitable candidates for sAVR and equivalent for 1-year mortality in patients who are deemed high-risk for sAVR, albeit with an improved quality of life within the first 6 months. Randomized clinical trials are assessing the value of TAVR in intermediate-risk patients. Registry studies will provide increasing insight into patients with bioprosthetic valve failure (valve-in-valve), bicuspid disease, low-gradient/low-output aortic stenosis, and in other clinical subsets not currently included in randomized clinical trials.

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References

1. Lindroos M, Kupari M, Heikkila J, Tilvis R. Prevalence of aortic valve abnormalities in the elderly: an echocardiographic study of a random population sample. J Am Coll Cardiol. 1993 Apr;21(5):1220-5.
2. Carabello BA, Paulus WJ. Aortic stenosis. Lancet. 2009 Mar 14;373(9667):956-66. Epub 2009 Feb 21.
3. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr., Faxon DP, Freed MD, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. J Am Coll Cardiol. 2006 Aug 1;48(3):e1-148.
4. Brown ML, Schaff HV, Sarano ME, Li Z, Sundt TM, Dearani JA, et al. Is the European System for Cardiac Operative Risk Evaluation model valid for estimating the operative risk of patients considered for percutaneous aortic valve replacement? J Thorac Cardiovasc Surg. 2008 Sep;136(3):566-71. Epub 2008 Jul 26.
5. Bittner HB, Savitt MA. Management of porcelain aorta and calcified great vessels in coronary artery bypass grafting with off-pump and no-touch technology. The Annals of thoracic surgery. 2001 Oct;72(4):1378-80.
6. Byrne JG, Aranki SF, Cohn LH. Aortic valve operations under deep hypothermic circulatory arrest for the porcelain aorta: "no-touch" technique. Ann Thorac Surg. 1998 May;65(5): 1313-5.
7. Boeken U, Schurr P, Feindt P, Litmathe J, Kurt M, Gams E. Cardiac valve replacement in patients with end-stage renal failure: impact of prosthesis type on the early postoperative course. Thorac Cardiovasc Surg. 2010 Feb;58(1):23-7. Epub 2010 Jan 13.
8. Boulton BJ, Kilgo P, Guyton RA, Puskas JD, Lattouf OM, Chen EP, et al. Impact of preoperative renal dysfunction in patients undergoing off-pump versus on-pump coronary artery bypass. Ann Thorac Surg. 2011 Aug;92(2):595-601; discussion 602. Epub 2011 Jun 25.
9. Brinkman WT, Williams WH, Guyton RA, Jones EL, Craver JM. Valve replacement in patients on chronic renal dialysis: implications for valve prosthesis selection. Ann Thorac Surg. 2002 Jul;74(1):37-42; discussion 42.
10. Byrne JG, Karavas AN, Filsoufi F, Mihaljevic T, Aklog L, Adams DH, et al. Aortic valve surgery after previous coronary artery bypass grafting with functioning internal mammary artery grafts. Ann Thorac Surg. 2002 Mar;73(4):779-84.
11. Bloomstein LZ, Gielchinsky I, Bernstein AD, Parsonnet V, Saunders C, Karanam R, et al. Aortic valve replacement in geriatric patients: determinants of in-hospital mortality. Ann Thorac Surg. 2001 Feb;71(2):597-600.
12. Bose AK, Aitchison JD, Dark JH. Aortic valve replacement in octogenarians. J Cardiothorac Surg. 2007 Jul 13;2:33.
13. Attias D, Himbert D, Ducrocq G, Détaint D, Al-Attar N, Iung B, et al. Immediate and mid-term results of transfemoral aortic valve implantation using either the Edwards SAPIEN transcatheter heart valve or the Medtronic CoreValve System in high-risk patients with aortic stenosis. Arch Cardiovasc Dis. 2010 Apr;103(4):236-45. Epub 2010 May 20.
14. Thomas M, Schymik G, Walther T, Himbert D, Lefèvre T, Treede H, et al. One-year outcomes of cohort 1 in the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) registry: the European registry of transcatheter aortic valve implantation using the Edwards SAPIEN valve. Circulation. 2011 Jul 26;124(4):425-33. Epub 2011 Jul 11.
15. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010 Oct 21;363(17):1597-607. Epub 2010 Sep 22.
16. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, et al.; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011 Jun 9;364(23):2187-98. Epub 2011 Jun 5.
17. Leon MB. Partner-2. Paper presented at: Transcatheter Cardiovascular Therapeutics 2011 Interventional Conference; 2011 Nov 7-11; San Francisco, CA.
18. Buellesfeld L, Gerckens U, Schuler G, Bonan R, Kovac J, Serruys PW, et al. 2-year follow-up of patients undergoing transcatheter aortic valve implantation using a self-expanding valve prosthesis. J Am Coll Cardiol. 2011 Apr 19;57(16):1650-7.
19. Tamburino C, Barbanti M, Capodanno D, Sarkar K, Cammalleri V, Scarabelli M, et al. Early- and mid-term outcomes of transcatheter aortic valve implantation in patients with logistic EuroSCORE less than 20%: A comparative analysis between different risk strata. Catheterization Cardiovasc Interv. 2012 Jan 1;79(1):132-40. Epub 2011 Dec 8.

20. Bosmans JM, Kefer J, De Bruyne B, Herijgers P, Dubois C, Legrand V, et al. Procedural, 30-day and one year outcome following CoreValve or Edwards transcatheter aortic valve implantation: results of the Belgian national registry. Interact Cardiovasc Thorac Surg. 2011 Jan 25;12(5):762-7.

21. Eltchaninoff H, Prat A, Gilard M, Leguerrier A, Blanchard D, Fournial G, et al. FRANCE Registry Investigators. Transcatheter aortic valve implantation: early results of the FRANCE (FRench Aortic National CoreValve and Edwards) registry. Eur Heart J. 2011 Jan;32(2):191-7. Epub 2010 Sep 15.

22. Moat NE, Ludman P, de Belder MA, Bridgewater B, Cunningham AD, Young CP, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. J Am Coll Cardiol. 2011 Nov 8;58(20):2130-8. Epub 2011 Oct 20.

23. Avanzas P, Muñoz-García AJ, Segura J, Pan M, Alonso-Briales JH, Lozano I, et al. Percutaneous implantation of the CoreValve self-expanding aortic valve prosthesis in patients with severe aortic stenosis: early experience in Spain. Rev Esp Cardiol. 2010 Feb;63(2):141-8.

24. Zahn R, Gerckens U, Grube E, Linke A, Sievert H, Eggebrecht H, et al.; German Transcatheter Aortic Valve Interventions-Registry Investigators. Transcatheter aortic valve implantation: first results from a multi-centre real-world registry. Eur Heart J. 2011 Jan;32(2):198-204. Epub 2010 Sep 23.

25. Meredith I, Walton T, Walters D, Ormiston J, Worthley S, Yong G, et al. Twelve-month results from the CoreValve Transcatheter Aortic Valve Australia-New Zealand Study. J Am Coll Cardiol. 2011;58(20):B39.

26. Moynagh AM, Scott DJ, Baumbach A, Khavandi A, Brecker SJ, Laborde JC, et al. CoreValve transcatheter aortic valve implantation via the subclavian artery: comparison with the transfemoral approach. J Am Coll Cardiol. 2011 Feb 1;57(5):634-5.

27. Ruge H, Lange R, Bleiziffer S, Hutter A, Mazzitelli D, Will A, et al. First successful aortic valve implantation with the CoreValve ReValving System via right subclavian artery access: a case report. Heart Surg Forum. 2008;11(5):E323-4.

28. Bruschi G, Fratto P, De Marco F, Oreglia J, Colombo P, Botta L, et al. The trans-subclavian retrograde approach for transcatheter aortic valve replacement: single-center experience. J Thorac Cardiovasc Surg. 2010 Oct;140(4):911-5, 915.e1-2.

29. Bojara W, Mumme A, Gerckens U, Lindstaedt M, Gotzmann M, Germing A, et al. Implantation of the CoreValve self-expanding valve prosthesis via a subclavian artery approach: a case report. Clin Res Cardiol. 2009 Mar;98(3):201-4. Epub 2009 Feb 13.

30. Bauernschmitt R, Schreiber C, Bleiziffer S, Ruge H, Mazzitelli D, Hutter A, et al. Transcatheter aortic valve implantation through the ascending aorta: an alternative option for no-access patients. Heart Surg Forum. 2009 Jan;12(1):E63-4.

31. Linke, Alex (Universität Leipzig Herzzentrum, Leipzig, Netherlands). Conversation with: Jeffrey Popma, M.D. (Interventional Cardiology Clinical Services, Beth Israel Deaconess Medical Center, Boston, MA) at EuroPCR. 2012 May 16.

32. Mack MJ, Holmes DR Jr. Formal Request for a Medicare National Coverage Determination (NCD): Transcatheter Aortic Valve Replacement (TAVR) Procedures [Internet]. Baltimore, MD: Centers for Medicare and Medicaid Services; 2011 Sep 22 [cited 2012 Apr 24]. Available from: http://www.cms.gov/Medicare/Coverage/DeterminationProcess/downloads//id257.pdf.

33. Daneault B, Kirtane AJ, Kodali SK, Williams MR, Genereux P, Reiss GR, et al. Stroke associated with surgical and transcatheter treatment of aortic stenosis: a comprehensive review. J Am Coll Cardiol. 2011 Nov 15;58(21):2143-50.

34. Caudron J, Fares J, Hauville C, Cribier A, Dacher JN, Tron C, et al. Evaluation of multislice computed tomography early after transcatheter aortic valve implantation with the Edwards SAPIEN bioprosthesis. Am J Cardiol. 2011 Sep 15;108(6):873-81. Epub 2011 Jul 7.

35. Abdel-Wahab M, Zahn R, Horack M, Gerckens U, Schuler G, Sievert H, et al.; German transcatheter aortic valve interventions registry investigators. Aortic regurgitation after transcatheter aortic valve implantation: incidence and early outcome. Results from the German transcatheter aortic valve interventions registry. Heart. 2011 Jun;97(11):899-906. Epub 2011 Mar 12.

36. Khawaja MZ, Rajani R, Cook A, Khavandi A, Moynagh A, Chowdhary S, et al. Permanent pacemaker insertion after CoreValve transcatheter aortic valve implantation: incidence and contributing factors (the UK CoreValve Collaborative). Circulation. 2011 Mar 8;123(9):951-60. Epub 2011 Feb 21.